

I. STUDIES OF THE REACTIONS OF
SUBSTITUTED DIKETOPIPERAZINES
II. A STUDY OF THE BERLINERBLAU
INDOLE SYNTHESIS

BY
RALPH LAWRENCE ROWLAND

B. Chem., University of Minnesota, 1942

M. S., University of Illinois, 1943

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE SCHOOL OF THE
UNIVERSITY OF ILLINOIS, 1945

URBANA, ILLINOIS

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PART I. STUDIES OF THE REACTIONS OF SUBSTITUTED DIKETOPIPERAZINES

INTRODUCTION

Snyder and Chiddix¹ reported the non-Markownikoff addition of hydrogen bromide, hydrogen chloride and hydrogen sulfide to the olefinic bonds of 3,6-divinyl-2,5-diketopiperazine. This discovery suggested that the dipetopiperazine ring might be an electronegative group. To test the validity of this consideration, several studies of reactions of substituted diketopiperazines have been made.

DISCUSSION

The nitration of 3,6-diphenyl-2,5-diketopiperazine was effected and the mixture of nitration products was oxidized to a mixture of nitrobenzoic acids. Analysis of the oxidation mixture according to the Ingold-Smith² modification of Holleman's method indicated the presence of 77 per cent *m*-nitrobenzoic acid. Since this corresponds to an overall conversion of 3,6-diphenyl-2,5-diketopiperazine to *m*-nitrobenzoic acid of 56 per cent, the diketopiperazine group is, under the conditions of the nitration in concentrated sulfuric acid, *m*-directing and accordingly electronegative. The isolation of the isomeric nitrobenzoic acids from the oxidation product substantiated the analysis results for *m*-nitrobenzoic acid. No *o*-nitrobenzoic acid could be detected and *p*-nitrobenzoic acid was isolated in quantities corresponding to 5 - 10 per cent of the theoretical yield.

The ease of substitution of the halogen atoms in 3,6-bis-(*p*-bromophenyl)-2,5-diketopiperazine was studied. These halogen atoms showed no indication of reactivity greater than that of the halogen atom in bromobenzene.

The condensation of 3,6-dimethyl-2,5-diketopiperazine with ethyl oxalate or benzaldehyde was attempted under a variety of conditions. In no case was any condensation product isolated.

Since those reactions in which the diketopiperazine ring behaved as an electronegative group were effected under conditions whereby the dipetopiperazine may form a salt with acid, it appears that not the diketopiperazine ring but the diketopiperazinium salt is strongly electron-attracting.

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¹ Snyder and Chiddix, J. Am. Chem. Soc. **66**, 1002 (1944).

² Ingold and Smith, J. Chem. Soc. **1938**, 905.

PART II.

II. A STUDY OF THE BERLINERBLAU INDOLE SYNTHESIS

INTRODUCTION

The synthesis of indole in low yield from aniline and α,β -dichloroether, chloroacetaldehyde, or chloroacetal was reported by Berlinerblau¹ in 1887. The failure to obtain indole from aniline and chloroacetal has subsequently been reported twice.² Recently the condensation of aniline and α,β -dichloroether has been reported as one of the better methods for the synthesis of indole although the yield was not reported.³ Interest in the synthesis of *Ar*-substituted indoles prompted a study of the reaction in the hope of applying it to the synthesis of bromo- and nitro-indoles.

DISCUSSION

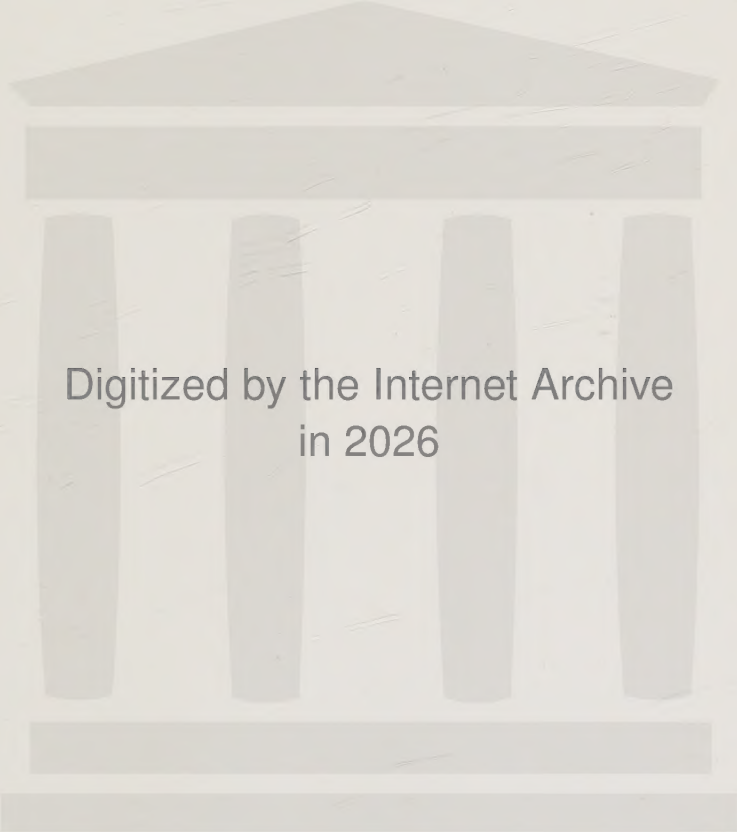
Attempts to synthesize indole from aniline and chloroacetal resulted only in high molecular weight compounds. From aniline and chloroacetaldehyde, indole was obtained in a 2 per cent yield and the condensation of aniline with α,β -dichloroether resulted in a 3 per cent yield of indole. Attempts to prepare 7-bromo-, 5-bromo-, 7-nitro-, 5-nitro-, and 5-methoxy-indoles from chloroacetaldehyde or chloroacetaldehyde hydrate and substituted anilines failed. An attempt to prepare *N*-benzylindole from chloroacetal and *N*-benzylaniline also failed.

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² Wohl and Lange, Ber., **40**, 4727 (1907);
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³ Treffler, Chem. Industries, **56**, **67** (1945).

VITA

The writer was born in LaCrosse, Wisconsin, on March 8, 1921. He was graduated from public high school in Houston, Minnesota, in 1938. The following fall he entered the College of St. Thomas, St. Paul, Minnesota. In 1940, he transferred to the University of Minnesota and was granted a Bachelor of Chemistry degree by that institution in June, 1942. He entered the University of Illinois during the summer term of 1942 and received a Master of Science degree in September, 1943. From September, 1942, to June, 1944, and from June, 1945, to September, 1945, he held a Special Research Assistantship. From June, 1944, to June, 1945, he held a teaching assistantship.



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